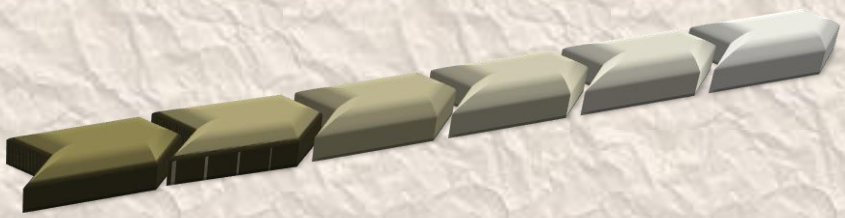
The spectrum of TB infection

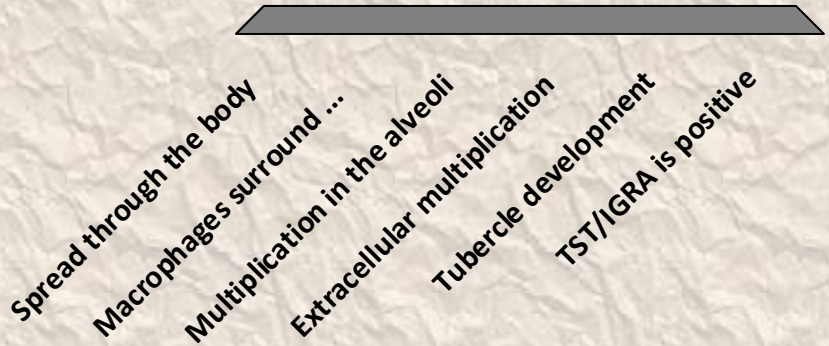
The beginning, the end and over again!



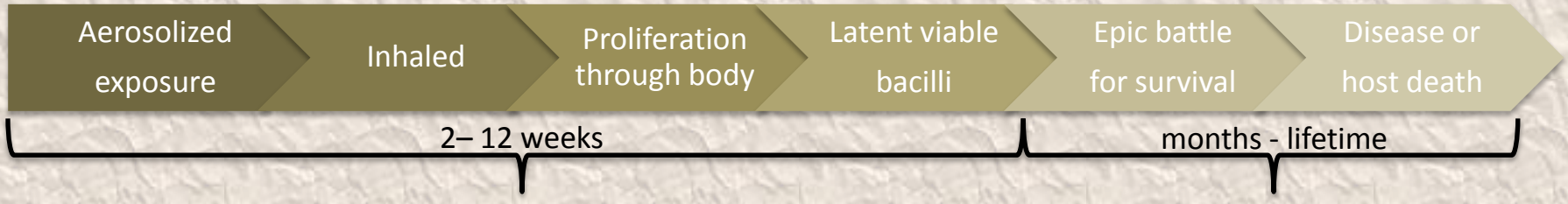
Place the 6 stages of TB pathogenesis in order of occurrence. TB bacilli is inhaled then…….

1. Spread through the body
2. Macrophages surround the bacteria
3. Multiplication in the alveoli
4. Extracellular multiplication
5. Tubercle development
6. TST/IGRA is positive

Answer: 3,1,2,6,5,4



How we understand progression



- Fatigue
- Night sweats and fever
- Loss of appetite & unexplained weight loss

- Cough
  - Length of time
  - frequency
  - Productive or dry
  - Continuous or intermittent
  - Hemoptysis
  - Seasonal

A changing paradigm

Some problems are so complex that you have to be highly intelligent and well informed just to be undecided about them.

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Acknowledgment

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Research: Man vs Animal

…there are substantial differences in immunological responses of humans not found or predicted in animal studies.

STATE OF THE

TUBERCULOSIS

TB or Not TB: That is

Robert L. Modlin[1,2]* and Barry R. Bloom[3]*

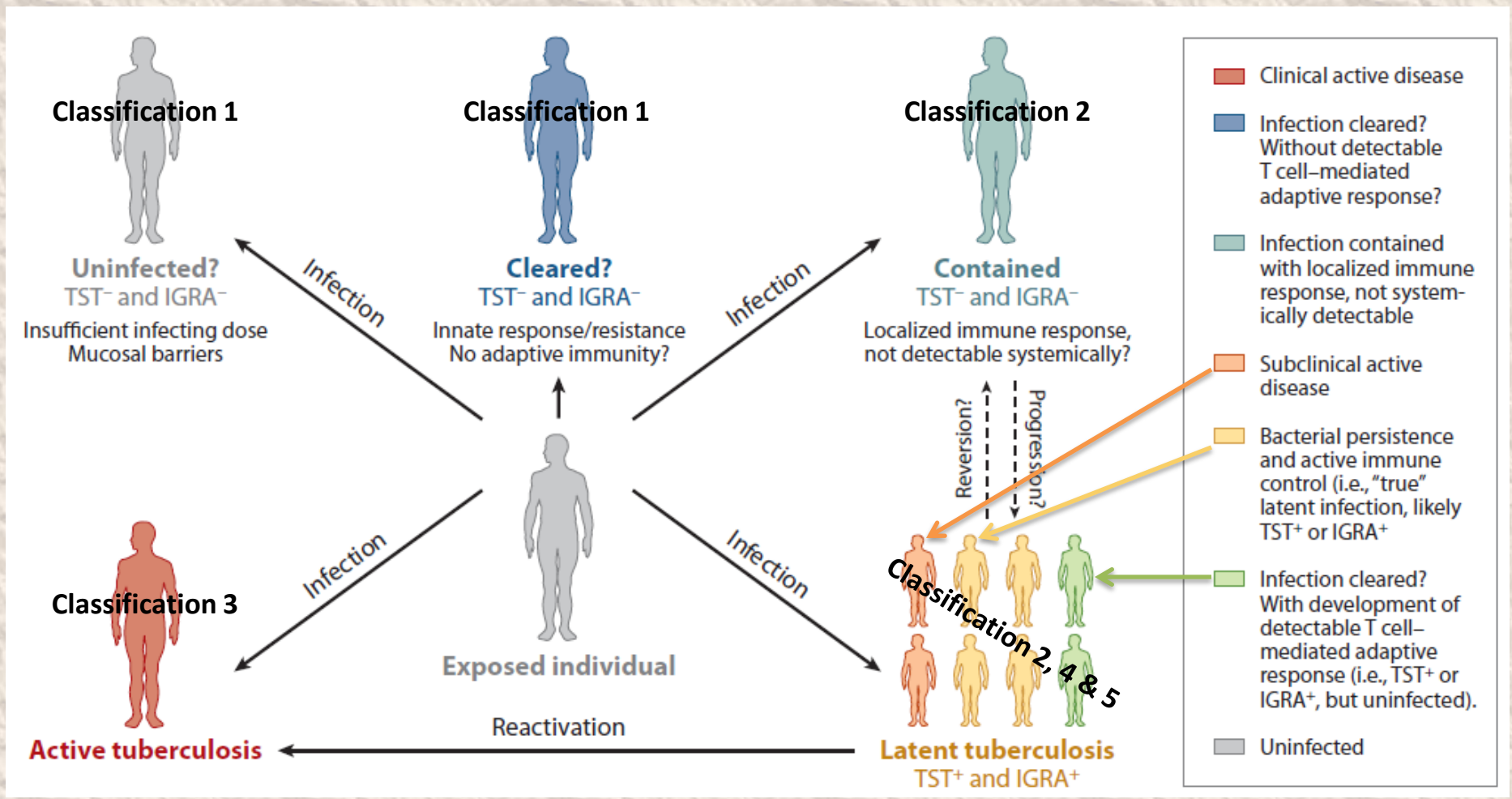
Tuberculosis (TB) remains a devastating infectious disease and, with the emergence of multidrug-resistant forms, represents a major global threat. Much of our understanding of pathogenic and immunologic mechanisms in TB has derived from studies in experimental animals. However, it is becoming increasingly clear in TB as well as in other inflammatory diseases that there are substantial differences in immunological responses of humans not found or predicted by animal studies. Thus, it is critically important to understand mechanisms of pathogenesis and immunological protection in humans. In this review, we will address the key immunological question: What are the necessary and sufficient immune responses required for protection against TB infection and disease in people—specifically protection against infection, protection against the establishment of latency or persistence, and protection against transitioning from latent infection to active disease.

Sci Transl Med 2013; 5:213.

The battle between M.*tb* and Us

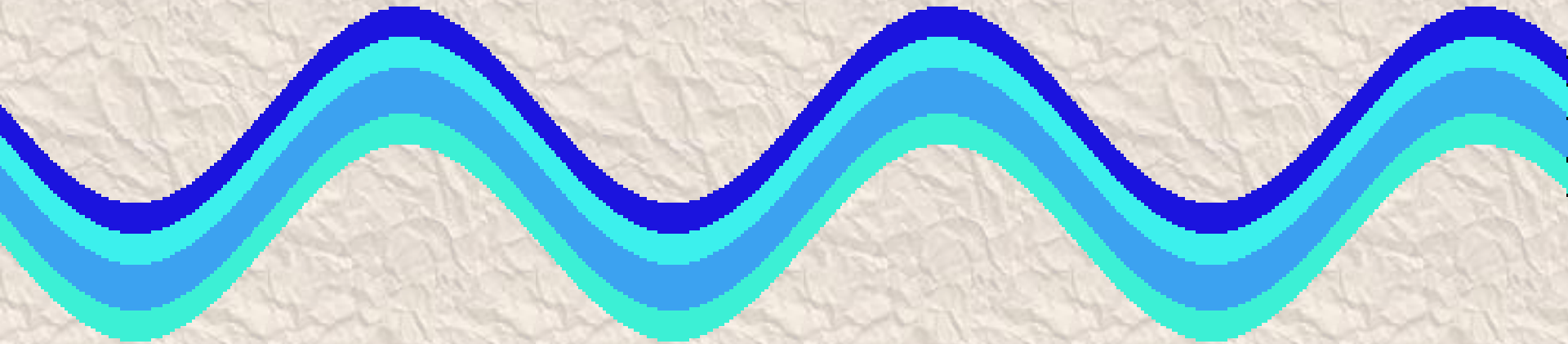
- **T**he **B**IG GUN:
  - It's ability to persist in hosts almost guarantees it's survival.
  - Persistence allows it to cause major lung pathology
  - Battle between our protective immune response (US) and the inflammatory response contributes to tissue damage and pathogenesis

A spectrum of TB infection exists!

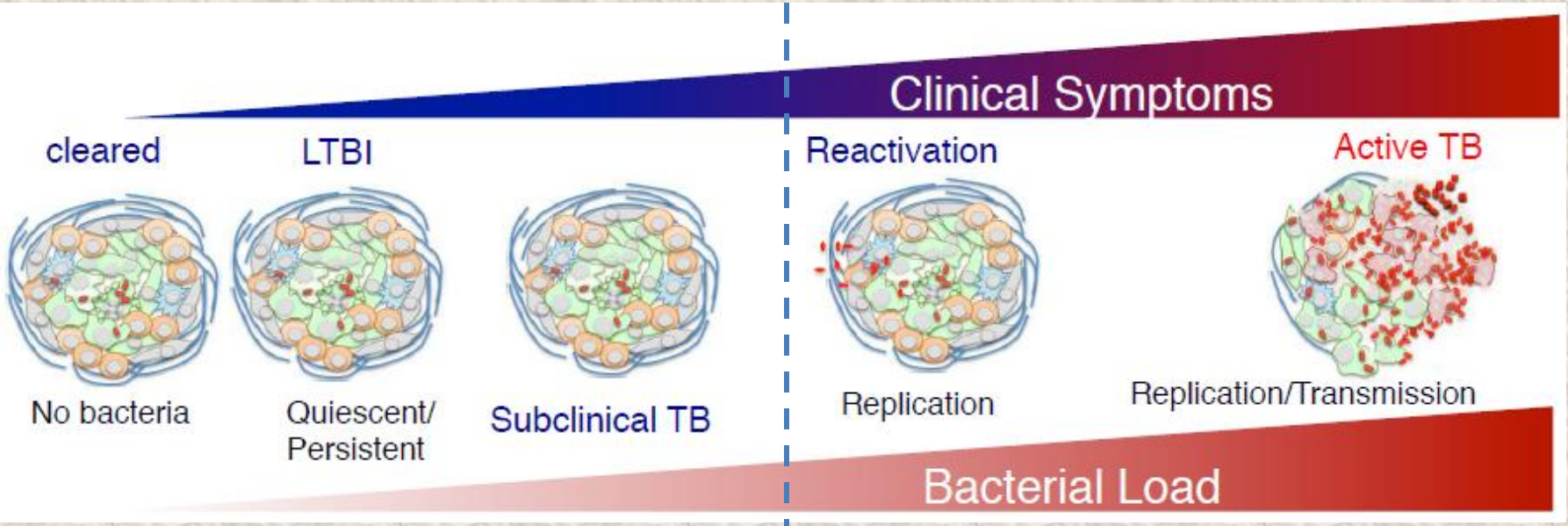


Shifting

"The classic dichotomy between active and latent disease is being reconsidered in favor of a continuous and dynamic spectrum extending from infection to disease that can coexist in the same individual."



"The spectrum of tuberculosis infection: New perspectives in the era of biologics" Rhematol May 2014 91:11-16.



M.*tb* can persist in the host for decades, localizing in many tissues and assuming difference metabolic states

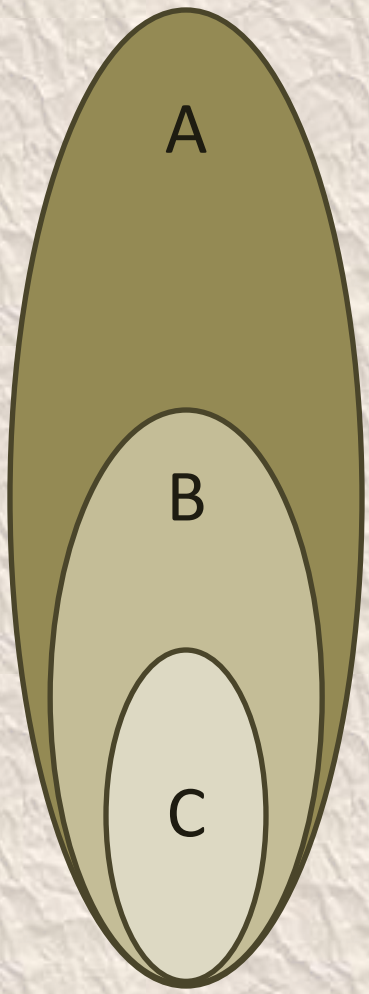
The bacilli may also replicate and multiply in vivo

Any event which impairs immune function leads to uncontrolled replication and TB disease

"Three population Model"

A,B,C

- Pop A: Rapidly multiplying (liquefied caseum)
  - Immense numbers of bacteria (cavities)
  - Most likely to mutate
  - Disease
- Pop B: Slowly multiplying (acidic environment)
  - Necrotic tissue
  - Disease
- Pop C: Brief & sporadic multiplication
  - Not sure where…. So everywhere?
  - Infection



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